

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference VTI/HSP/V171	FOR FURTHER ACTION		See item 4 below
International application No. PCT/EP2004/052962	International filing date (<i>day/month/year</i>) 15 November 2004 (15.11.2004)	Priority date (<i>day/month/year</i>) 13 November 2003 (13.11.2003)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant VIB vzw			

<p>1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.</p>																								
<p>3. This report contains indications relating to the following items:</p> <table> <tbody> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </tbody> </table> <p>4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).</p>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of issuance of this report 15 May 2006 (15.05.2006)	
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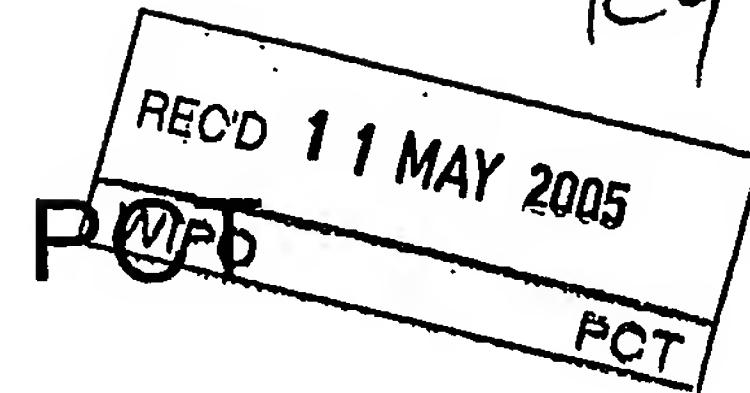
PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

26/5



WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Applicant's or agent's file reference see form PCT/ISA/220		Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet)	
International application No. PCT/EP2004/052962		International filing date (day/month/year) 15.11.2004	
International Patent Classification (IPC) or both national classification and IPC C12Q1/68			
Applicant VIB VZW			

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1b/s(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material:
 - in written format
 - in computer readable form
 - c. time of filing/furnishing:
 - contained in the international application as filed.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/052962

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-3,5-11
	No: Claims	4
Inventive step (IS)	Yes: Claims	1-3,5-9
	No: Claims	4,10,11
Industrial applicability (IA)	Yes: Claims	1-11
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

I. Basis (Continuation)

3.1 The Sequence listing pages 1-4 filed with the letter of 09/03/2005 do not form part of the application (Rule 13^{ter}.1(f) PCT).

V. Reasoned statement (Continuation)

2.1 CITATIONS

Reference is made to the following documents:

D1: BENNDORF RAINER ET AL: "HSP22, a new member of the small heat shock protein superfamily, interacts with mimic of phosphorylated HSP27 (3DHSP27)" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 276, no. 29, 20 July 2001 (2001-07-20), pages 26753-26761, XP002325897 ISSN: 0021-9258

D2: TIMMERMAN V ET AL: "Distal hereditary motor neuropathy type II (distal HMN type II): phenotype and molecular genetics." ANNALS OF THE NEW YORK ACADEMY OF SCIENCES. 14 SEP 1999, vol. 883, 14 September 1999 (1999-09-14), pages 60-64, XP002325638 ISSN: 0077-8923

D3: IROBI JOY ET AL: "Hot-spot residue in small heat-shock protein 22 causes distal motor neuropathy." NATURE GENETICS, vol. 36, no. 6, June 2004 (2004-06), pages 597-601, XP002325639 ISSN: 1061-4036

2.2 NOVELTY (Art. 33(2) PCT)

2.2.1 D1 discloses the cloning of the HSP22 gene but not the polymorphisms that are associated with HMN II. Since the fragments of claim 4 do not necessarily contain a polymorphism, D1 is novelty destroying for claim 4.

2.2.2 D2 discloses that the gene causing autosomal dominant distal hereditary motor neuropathy type II (HMN II) is located on chromosome 12q24.3. A yeast artificial chromosome (YAC) contig map spanning the candidate region has been constructed to isolate the gene responsible for distal HMN II. Positional and functional candidate genes are currently being screened for the presence of mutations in distal HMN II patients. D2 does not disclose the polymorphisms in the HSP22 gene which are associated with HMN II.

2.2.3 The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claim 4 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

2.3 INVENTIVE STEP (Art. 33(3) PCT)

2.3.1 Document D2 is considered to represent the most relevant state of the art (cf 2.2.2). The subject-matter of claim 1 differs in that polymorphisms (cf Table 1) in the HSP22 gene are associated with HMN II.

2.3.2 The problem to be solved by the subject matter of claim 1 may therefore be regarded as providing a genetic diagnosis for HMN II. The solution would be any of the polymorphisms disclosed in Table 1.

2.3.3 This solution was not known nor hinted to in the prior art and would not be obvious for the skilled person.

2.3.4 Claim 10 refers to the use of HSP22 for the manufacture of a medicament for the treatment of HMN II. However, the application does not provide support to show that the use of HSP22 results in a treatment of HMN II. Since it is not shown that the use of HSP22 solves the problem posed, the present claims 10 and 11 are not inventive.

2.3.5 The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of claims 4, 10, and 11 does not involve an inventive step (Rule 65(1)(2) PCT).

VIII. Certain Observations (Continuation)

- 1 Claims 1,2,4-7,9 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempts to define the subject-matter in terms of the result to be achieved "a mutation indicative of distal hereditary motor neuropathy type II" which merely amounts to a statement of the underlying problem. The technical features necessary for achieving this result are however missing (mutations set forth in Table 1).
- 2 The first column of Table 1 refers to the nucleotide numbering of the polymorphisms in the HSP22 gene. This numbering however does not seem to be in line with the corresponding amino acid changes referred to in the second column of Table 1. Based on these data and on figure 3, the corresponding nucleotide positions in SEQ ID NO:1 seem to be 241G>T, 429A>G, and 431G>C. Further processing of the application will therefore be based on these positions in SEQ ID NO:1.
- 3 Claim 7 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. Claim 7 reads "A method for the preparation of a diagnostic assay" but does not contain any technical feature for the preparation of such an assay.
- 4 Claims 3 and 8 contain a reference to the description (i.e. Table 1). According to Rule 6.2(a) PCT, claims should not contain such references except where absolutely necessary, which is not the case here.
- 5 Claims 10 and 11 are not supported by the description as required by Article 6 PCT, as their scope is broader than justified by the description and drawings. The reasons therefor are the following: The application does not provide any support to show that the use of HSP22 results in a treatment for HMN II.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.
PCT/EP2004/052962